that interesting work secures repetition of movements without unduc fatigue. Not only must the physician take into consideration, therefore, the type of movements produced by the work which he is about to prescribe, but also the desires and interests of the patient.

We found that the soldiers in the hospital took kindly to occupational therapy, and often in spite of their disabilities produced work which from an artistic and technical point of view was of a high order. From a study of these cases over a period of more than a year it became evident that the results of this form of treatment entitle it to an important place among the therapeutic agents at our disposal in the treatment of injuries presenting paralysis, contracture, fibrosis or lack of coördination. In view of the fact that occupational therapy has been proved to be of definite value in the treatment of various other conditions, possibly the day is not far distant when an occupational therapy department, under a trained supervisor, will be recognized as a necessary part of the equipment of every up-to-date hospital.

SOME OBSERVATIONS ON THE USE OF ARSPHENAMIN: ITS EFFECT ON THE KIDNEYS AND ITS THERAPEUTIC RESULTS.

BY HORACE B. ANDERSON, M.D., PENNSYLVANIA HOSPITAL, PHILADELPHIA.

RECENT medical literature is pregnant with articles either extolling the virtues of salvarsan and arsphenamin by reporting series of cases in which observations on the clinical manifestations and serologic reactions have indicated the therapeutic value of the drug or abusing and condemning the use of it by reporting all manner of reactions varying from the mild vasomotor disturbances to fatalitics. It is the purpose of this paper to do neither the one thing nor the other, but rather to take the opposite ground; to submit some evidence, after studying 39 cases which have had twenty or more doses of arsphenamin, to show the non-toxic effect of the drug on the kidneys when administered in therapeutic doses over a comparatively long period of time and at the same time to give some data concerning its value as a therapeutic agent.

Concerning the gross and histopathologic changes of acute arsphenamin poisoning we have already acquired considerable information from the studies and reports of Kolmer' and others, but concerning the chronic poisoning we have less information largely because of the comparatively recent use of the drug. In the future, no doubt,

¹ AM. JOUR. MED. Sc., 1920, clx, 188.

we will have a more accurate knowledge of the pathologie effects of its prolonged use and can come more nearly answering the important question, "What changes are produced in the kidneys by the prolonged use of arsphenamin?" One only appreciates the importance of such a question when he reflects on the fact that thousands of doses of arsphenamin are being administered every day to patients throughout the country and by the energetic application of their plans to eradicate syphilis the U. S. P. H. Service and the State boards of health are increasing daily the number of patients treated.

In this clinic prior to 1918 it was the policy to give weekly injections continuously as long as the patients would submit to it and the Wassermann reaction was positive. Since that date the policy has been to administer a course of arsphenamin consisting of six weekly injections, the dose being, unless contra-indicated, I decigram per thirty pounds body weight followed by a ten weeks' course of mercury in the form of the inunctions, the protoiodides or injections of the salicylate of mercury and after this a rest of one month without treatment. During the second and third year the same plan of treatment is used, but the duration of the course is modified somewhat to meet the clinical aspect of the case, the serologic findings and the mental attitude of the patient.

Wassermann tests are taken every second week while arsphenamin is being given and at the end of each course of mercury. Acetone insoluble and alcoholic extract reinforced by cholesterin antigens are used in all tests.

It was possible to study the kidney function of 39 patients who had had over twenty doses of arsphenamin. The phenolsulphone-phthalein tests were performed after the method of Rowntree and Geraghty,² the urea nitrogen, non-protein nitrogen and ereatinin after the method of Folin and Wu³ and those cases that showed albumin in the urine by the heat and nitrie acid tests were further tested for globulin by the use of ammonium sulphate, etc., as described by Hawk.⁴ The data of kidney function tests is given in Table I.

The average number of treatments for these 39 eases is approximately 30 doses, consisting of 4.6 deeigrams each distributed over a period of a little over two years. To state it another way these patients have had an average of 14 treatments of arsphenamin per year for about twenty-six months. The preparations used have varied but in the main consisted of arsenobenzol, "Billion" arsphenamin, Metz and all later treatments have been of arsphenamin made by the Dermatological Research Laboratory of Philadelphia.

Jour. Pharm. and Exper. Therap., 1910, i, 579.
 Jour. Biol. Chem., 1919, xxxviii, 81.

Pract. Phys. Chem., 1918, 6 ed., p. 454.

TABLE I.

	:		-		ation ment.	phe	seot nol- aleiu put.		nalitative uri fter last tre				Presen blood mioat	
Case No.	His- tory No.	No. of doses.	No. of gms.	Year.	Months.	First hour,	Second pour.	Specific gravity.	Albumin.	Casts.	Sugar.	Non-protein N.	Urea N.	Creatinin.
1 23 4 5 6 7 8 0 10 11 12 13 14 15 16 17 18 19 20 21 22	245 251 281 281 566 660 637 432 410 370 687 810 681 333 344 33 37 64 109	32 24 50 27 52 29 29 28 38 38 34 39 20 21 23 24 29 29 20 21 25 25 25 25 26 27 27 28 29 29 29 42 29 44 29 44 29 44 29 44 29 44 44 29 44 44 44 44 44 44 44 44 44 44 44 44 44	12.0 17.5 20.8 13.0 20.0 15.4 13.8 12.0 14.2 15.0 11.7 20.0 15.0 8.0 7.2 12.0 7.2 13.0 12.0 13.0 14.0 15.0 15.0 15.0 15.0 15.0 15.0 15.0 15	1110134 .1213539221141 4	749272506180202562521 5	50 60 55 60 55 55 30 70 55 125 25 60 60 60 60 60 60 60 60 60 60 60 60 60	18 13 18 23 18 15 15 15 120 20 12 13 18 13 15 10 11 10 11 10 11 10 10 10 10 10 10 10	1020 1020 1020 1012 1012 1012 1025 1025	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000	000000000000000000000000000000000000000	33 32 27 33 30 28 46 34 33 25 31 28 37 32 34 30 28 27 28 31 32 32 34 33 32 34 34 35 36 36 37 37 38 38 38 38 38 38 38 38 38 38 38 38 38	12 15 17 12 13 14 17.5 16 10 17 12 17 12 13 14 20 14 12 20	1.6 1.8 2.2 1.6 2.0 2.0 1.5 1.8 1.5 2.0 1.7 2.2 2.0 1.7 2.2 2.0 1.7 2.2 2.0 1.7 2.2 2.0 1.7 2.2 2.0 1.7 2.0 1.0 1.7 2.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1
23 24	215 220	35 22	15.7 9.35	2	11	70 55	10 20	1015 1025	1r., none	0	8	35 37	13 20	2.0 1.3
25	123	33	13,2	1	0	25	15	1018	Dis. tr.; ue glob.	gr.	0	37	17	1,6
26 27 28 29	758 582 205 595	34 31 21 22	15.6 12.8 11.5 11.0	1 1 2	8	60 60 55 30	15 10 15 15	1024 1021 1020 1012	Cloudy, nlb. and glob.	0 0	0	33 35 35 20	12 17 17 14	1.6 1.5 1.7 1.6
30 31 32 33 34 35 36 37 38 39	585 240 275 232 106 18 597 050 217 258	32 34 20 20 28 23 20 20 21 20	15.1 15.5 7.0 0.0 13.8 11.5 12.1 10.0 10.4 13.4	1 1 2 1 1 1 2 1 2 1	0 11 1 4 11 2 1 1	30 60 60 55 55 55 60 05	15 15 10 15 20 10 20 15 15	1015 1025 1015 1020 1024 1024 1020 1018 1010 1020	0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000	29 31 42 40 40 31 29 33 37 33	14 13 15 20 18 17 13 14 10	1.7 1.6 1.6 1.7 1.7 1.7 1.7 1.6 1.6 1.8

A table giving the araphenamin received, the duration of treatment, the phenoisulphocephthalein output of the kitneys and the urine and blood examination of patients having had twenty or more doses of araphenamin.

With the exception of patient No. 25, who was transferred from the medical clinic, where he was first seen and diagnosticated tabes and nephritis, there is no conclusive p oof of an existing nephritis in any of these cases. At that time and at all subsequent examinations the urine of patient No. 25 showed some casts and albumin. His condition apparently is no worse now than when treatment was first instituted. Judging from the phenolsulphonephthalein output and he albumin and easts in the urine this patient has some nephropathy, but the evidence is in favor of its having been acquired prior to treatment. Patients Nos. 6, 21, 24 respectively show a trace of albumin at one examination, but there is no other evidence of a nephritis. Patient No. 29 shows a cloud of albumin, but when appropriate tests were used it was discerned that more than 50 per cent. of the protein precipitate was globulin. This case is well clinically, shows no other evidence of nephritis in the other examinations and therefore might be a case of non-nephritic proteinnria.

The data of table No. 1 lead in general to the conclusion that no demonstrable kidney damage has been done. There is, of course, nothing to show whether or not there has been any limitation of the wide factor of safety which the kidney naturally possesses. Several of the patients show a decreased phthalein output which

one may interpret as one will.

The efficiency of any new system of treatment must be determined ultimately by the Wassermann reaction, for it has long been known that negative clinical manifestations are no guide to the patient's

potential syphilitic state.

The teclinic employed in our laboratory for doing Wassermann tests has been modeled after that described by H. K. Detweiler. We use, however, only 0.1 c.c. of patient's serm and use the waterbath instead of dry heat for ineubation. Detweiler's method of daily titrations of the complement as well as the amboceptor has proved very satisfactory. The antisheep hemolytic system is employed.

Two antigens are used, the acetone insoluble and the cholesterin reinforced alcoholic extract, made after the method described by Kolmer.⁶ These antigens are titrated every six weeks for their antigenetic and anticomplementary values. The former is tested on the pooled sera of patients who both clinically and serologically

are luetic.

In our experience with cholesterized antigen it is the more sensitive and the last to become negative. The acetone insoluble is far more liable to be a correct index to the true condition when positive, but often fails to give a positive reaction in the early and late stages and also after a limited amount of treatment. This fact is demonstrated in Tables III, IV and V. Although it is true that a cholesterinized antigen will not infrequently give a false positive reaction, we believe it is the most valuable antigen that can be employed as a guide to treatment.

⁵ Am. Jour. Syph., 1918, ii, 120-137.

Inf. Immunity and Spec. Ther., 1917, 2d ed., p. 446.

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	No. of doges	persistent neg. Wass.	21 0 Wass. pos.	26 43 Wass. pos. Wass. pos.	3,4	Wass. pos.	81-
		admission.	St. pos. St. pos. St. pos.	Positive St. pos. St. pos. Positive	Wk. pos. St. pos.	St. pos. St. pos.	Positive St. pos.
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Diabetes insipidus	Ulcer of penis	Interstitial keratitis	Leg ulcers Mucous patches in	mouth Pain in heels	Tabes ?		Luctic sore-throat	Chancre weakness	Leg ulcers	Myocarditis	TO CONTINUE MOLITIES	Rash To be cured		Rush: mucous patch	Chanere Body pains	To be cured	Macular eruption
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A table giving a summary of the history, treatment and present condition of the patients of Table I.

TABLE III.—IN THESE TEN CASES THE CHOLESTERINIZED ANTIGEN IS
APPARENTLY MORE SENSITIVE THAN THE ACETONE
INSOLUBLE ANTIGEN.

												-								
Case No.		1	:	2		3		4		5		6		7		В	,	D	1	0
His- tory No.	8	99	P.	P.	96	10	10	3 0	10	юз	10	86	10	43	9:	86	19	67	10	49
Lesion	Cha	ncre.	Cha	ncre.	Cha	ncre.	Ea seco	rly ond- ics.	Cha	nere.	Cha	nere.	Es seco	rly oad- ies.	Cha	nere.	Chu	acre.	Er	np. ular.
Weekly injec. arsphenamin	W	388,	W	155.	W	158,	W	185.	W	0.89.	W	nas.	w	183.	W	188.	W	138.	W	355.
Week!	c.	A.	C.	A.	C.	A.	c.	λ.	c.	A.	C.	A.	C.	Α,	c.	A,	C.	А.	c.	A.
1 9	2	1	2	-	1	-	4	-	4	3	4	1	4	2	4	-	3	-	3	-
1 2 3 4 5 6	- 4 1	= ::	1 :-	- :1 :	- :- :-	- :- :-	4 1 2 	1 - Tw	3	3 3	l 	 	4 :- cury	1 :- :-	2	:-	1	-	1	1
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TABLE IV.—IN LATE STAGES OF SYPHILIS THE CHOLESTERINIZED ANTIGEN SEEMS TO BE MORE SENSITIVE IN SOME CASES.

					·															
Case No.		ı		2		3		1		5		6		7		8	,	Ð	1	0
His- tory No.	19	21	10	48	19	19	19	27	90	34	9	63	10	78	9	51	9	76		1
Lesion	Lat	ent,	lle pai	dy ns.	Ui	er.		eu• r.	Lat	ent.	Lat	ent.	טוט	er.	Bo	nly ins.	וט	cer.	Lat	ent.
Weekly injec. arsphenamin	W	155.	W	ISĐ.	w	135.	Wa	155.	w	155.	W	nss.	w	198.	W	nsa.	w	nss.	W	189.
Weekly arsplic	C.	A.	C.	A.	c.	Α.	c.	λ.	C.	A.	C.	A.	c.	A.	c.	A.	c.	A.	C.	A
1 2 3 4 5	3	- -	4 3	- 1	4	- 1	3 2	-	4 3	2	4	- 1	1	- 1	4	- -	4	3	4	1 2
5 6 15	3 2	1	3	ï	4	ï	4	- Tw	o In			2 reur	2 y 1	-	4	_	4	1	3	_
16 17 18 19		.	:: ::	::	::		::	::	:-	: 1:	3	-	::		::	:. ::	4	1	-	-
20 20	::	::	::	::	::	::	::	::	:: '		::	::	::	::	::	::	::	::	_	-

Tables giving the Wassermann reactions with acctone insoluble antigen (A) and cholesterinized alcoholic extract antigen (C). The figures 1 to 4 mean Wassermann 1 to 1 plus, — implies a negative Wassermann. The specimens of blood were taken at the time of the weekly injection of araphenamin.

TABLE V.—UNDER TREATMENT THE CHOLESTERINIZED ANTIGEN OFTEN
REMAINS POSITIVE AFTER THE ACETONE INSOLUBLE ANTIGEN
HAS BECOME NEGATIVE.

Case No.		1		2		3		4		5		6		7		8		9		10
llis- tory No.	8	886 ~	2	22	8	91		8	1	02	8	80	4	27	4	42	5	67	9	76
Lesion	Ch	ancre	Sec	ond- ics.	Spo	ndy- tis.	Sec	ond-	Mu	cous ches.	1	mmn of num.	R	ısh.		icu-		eous		er of
Weekly injec. arsphenamin	W	nss.	W	A85.	W	888.	w	naa.	w	nsa.	w	A39.	W	888.	w	0.99.	W	B\$5.	W	nss.
Weekly arsphe	C.	A.	C,	A.	c.	A.	C.	A.	C.	A.	c.	A.	c.	A.	c.	A.	C.	Α.	c.	A.
1 2 3 4 5	4	4 4 4	4	4 4 3	4	4	4	4 4	4	4	4	4 3	4	4	4	4	4	4	4	4
- 1	3	ï	2	0	4	ï	 4 3	Tw		4 onth	4 a of	4 1 mer	4 2 cury	2	4	4 2	::	::	4 2	l l
15 16 17 18	::	- :- :-	::	:: ::	3	ï	<u>:-</u>	:- ::	4	- :	3	:: :-	4	ï	2 	3 	4	-		
19 20 20	::				4	ï 	::	Tw	o m	onth	ol o	mer	4 cury	2	4	=	1	=	4	-
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	. 1	(:: 1		.::]	.:.]			<u> </u>	j					2	-	-	-!	- 1	

Tables giving the Wassermann reactions with acetone insoluble antigon (A) and cholesterinized alcoholic extract antigon (C). The figures 1 to 4 mean Wassermann 1 to 4 plus, — implies a negative Wassermann. The specimens of blood were taken at the time of the weekly injection of arsphenance.

When we make a study of Table II we find 17 of the 39 cases have now had a negative Wassermann reaction for a year or more. Nine of the group have had a negative reaction for less than one year and 13 of the 39 cases continue to have weakly positive and strongly positive reactions. Of those with persistently negative reactions for a year or more 2 were in the primary stage, 4 were in the secondary and 11 in the tertiary and latent stages. The average number of closes to produce persistently negative Wassermann reactions in this group was 18.7, for those in the primary stage 12, for those in the secondary stage 12.7 and in the tertiary and latent stages 21.3 closes.

For the 39 patients the average salvarsan per patient has been 136 deeigrams and the average time of treatment one hundred and seventeen weeks. This treatment has resulted in making 17 out of the 39, or 43 per cent. of the patients clinically and serologically negative for a year or more. Seven more patients, 18 per cent., have had more than two persistently negative Wassermanns, so

that, on the whole, more than half of these 39 patients already have a very favorable outlook as far as the ultimate outcome of their treatment is concerned. This 61 per cent. of the patients has had an average of 4.9 courses of six weeks of mercury in some form or other.

TABLE VI. SECONDARY STAGE.

Case No.	History No.	Number of positive Wassermanns	Decigrams arsphensmin to first persistent aegative Wassermann.	first persist- ent negative	Total arsplienamia.	Total weeks.	Number of persistent negative Wassermanns
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 17	1 172 315 247 257 324 929 914 412 567 843 635 855 738 870	12222343544335224	53 40 45 45 49 35 38 39 51 20 67 57 45 57 47 142	20 20 20 18 32 10 28 18 20 4 56 30 30 30 44 39	68 89 61 73 92 48 70 78 56 67 90 60 60 65 47	52 44 21 70 82 56 28 24 39 56 52 36 44 42	3 4 2 5 5 5 3 4 2 4 6 3 6 1 3 1 1 2

A table giving the arsphenamin and Wassermann records of patients starting treatment in the secondary stage. The time under observation for these patients is short and their ultimata status is still uncertain.

TABLE VII.-TERTIARY STAGE.

Case No.	History No.	Number of positive Wassermanns	Decigrams arsphenamin to first persistent negative Wassermann,	first persist- ent negative	Total arsphenamin.	Total weeks.	Number of persistent negative Wassermanns
1 2 3 4 5 6 7 8 9	4 183 290 260 880 416 452 553 867 713 807	4 1 2 3 4 4 4 1 1 3 2	05 57 60 96 40 34 72 77 40 59	237 102 40 116 29 48 72 48 34 34 31	95 57 00 96 45 59 98 109 04 60	237 102 48 178 20 80 92 76 42 45 38	1 1 3 2 1 2 3 5 5 5

A table giving the arspheaumia and Wassermann records of patients starting treatment in time tertiary stage. These patients are to be classed with those of Table VI in respect to observation

In Tables 6 and 7, which are composed of cases now negative that presented secondary and tertiary lesions on admission, and in the majority of cases more than one positive Wassermann reaction, I believe we get a fair index as to the efficiency or inefficiency, as you may choose to call it, of our present method of treatment. The average amount of treatment necessary to produce the first persisting negative Wassermann reaction in the group of secondary

cases was 52 decigrams and the average time twenty-eight weeks. That is to say, they received 10.2 doses of arsphenanin consisting of 5 decigrams each. The average case, therefore, in this group did not give a persisting negative reaction until near the end of the second course of treatment.

It took an average of 62 decigrams to produce a persisting negative Wassermann reaction in the tertiary group. The time averaged seventy-two weeks. This means that it was during the third course of arsphenamin that they began to show a negative reaction. This at first seems better than the situation with the patients of Table II, but it is to be understood that for the patients of these latter tables more relapses may be expected. We frequently see patients who having received six to twelve doses of arsphenamin have been discharged with a negative Wassermann only to return within about a year both clinically and serologically positive.

Summary. 1. Because of its extensive use at present it is highly important that we know more perfectly the effects of the prolonged

use of arsphenamin on the kidneys.

2. Kidney functional tests on 39 cases after they have received thirty do es of arsphenamin, each dose consisting of 4.6 decigrams, and distributed over a two-year period, fail to give any conclusive

evidence of injury to the kidneys.

3. The efficiency of any method of treatment must ultimately be determined by the Wassermann reaction. It is more trustworthy to use at least two antigens; the acetone insoluble antigen is a safe guide to diagnosis and the alcoholic extract reinforced by cholesterin is an excellent guide to treatment.

4. It is impossible to say how much arsphenamin and how many courses of mercury may be necessary to produce a negative Wasser-

mann reaction in any given case.

5. Six injections of arsphenamin and one course of mercury, the amount too often prescribed by certain groups of physicians, may produce one negative Wassermann reaction, but the average case of secondary or tertiary syphilis will require twelve or more doses of arsphenamin and a corresponding amount of treatment with mercury to produce a negative Wassermann reaction, and one which only with further treatment may reasonably be expected to persist.